Symmetry: Culture and Science
Vol. 4, No. 1, 1993, 83-92

CHIRALITY OF ORGANIC MOLECULES

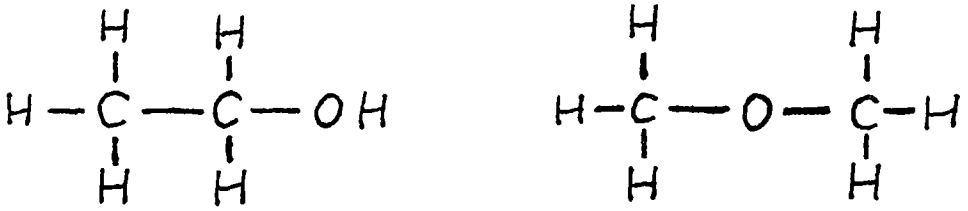
Ferenc Glück

Theoretical physicist, (b. Bánd, Hungary, 1963).
Address: Central Research Institute for Physics, Budapest 114, P.O. Box 49, H-1525 Hungary.
Fields of interest: Particle physics, weak interaction, radiative corrections.
Publications: Radiative correction to electron neutrino correlation in lambda β-decay, (with Tóth, K.), *Physical Review*, D40, 1989, 119; Order-α radiative corrections for semileptonic decays of unpolarized baryons, (with Tóth, K.), *Physical Review*, D41, 1990, 2160; Order-α radiative corrections for semileptonic decays of polarized baryons, (with Tóth, K.), *Physical Review*, D46, 1992, 2090; Measurable distributions of unpolarized neutron decay, *Physical Review*, D47, 1993, 2840.

Abstract: *A summary of the optical isomerism of organic molecules and of the bioorganic optical purity (biomolecular handedness) is given. The origin of the optical purity is explained by means of spontaneous symmetry breaking and the parity violating weak interaction.*

1. OPTICAL ISOMERISM IN ORGANIC CHEMISTRY

Generally, isomers are compounds with the same molecular formula which differ in at least one chemical or physical property. For example, two isomers corresponding to the C_2H_6O empirical formula:



Ethanol

Dimethyl ether

Figure 1:

There are several kinds of isomerism (chain, position, geometrical, etc.). The determination of the shape of the molecules and the relative arrangement of its parts in space is the most important task in organic chemistry.

Optical isomerism

Molecules that exist in two different forms related as object and mirror image are called *optical isomers* (enantiomers). The spatial structure of these molecules is asymmetrical: they have neither planes of symmetry, nor centers of symmetry. They are said to be *chiral*. Chirality refers to the 'handedness' or the screw sense (left or right) of an object. Those objects that are not identical with their mirror images are said to possess chirality, or handedness (familiar examples are hands or screws).

Molecules containing four nonidentical atoms or groups of atoms linked to a central carbon atom provide a typical example for optical isomerism. The carbon atom in these molecules is often called *asymmetric*. The picture below shows the general structure of the two enantiomers:

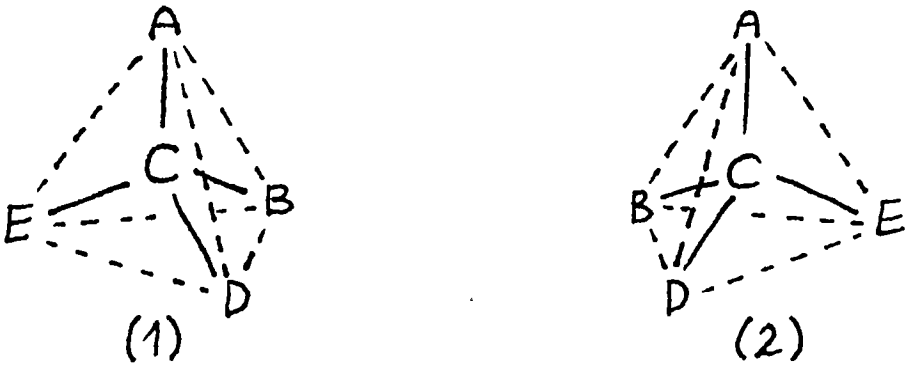


Figure 2

Here the *A*, *B*, *C* and *E* groups sit in the vertices of a regular tetrahedron, the *C* carbon atom is in the centre. The tetrahedral orientation of the carbon valencies is essential for this molecular structure.

The planar representation of the above configurations is the following (Bentley, 1969):

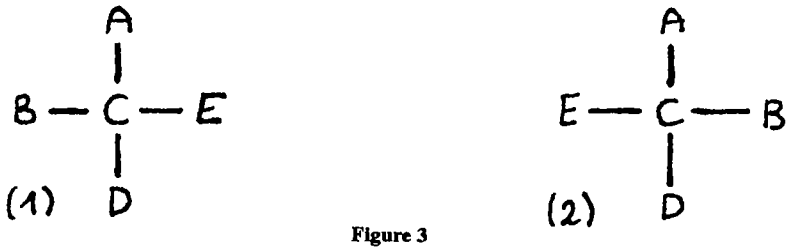


Figure 3

Optical activity

The optical isomer molecules are capable of rotating the plane of polarization of linearly polarized light (Glück, 1993; Section 6). They are said to be optically active. The two enantiomers rotate the plane of polarization in opposite directions, with the same angle. We denote the enantiomers rotating the plane in clockwise direction by the + symbol, the others by $-$.

The optical activity of organic compounds provides many important applications. If a linearly polarized light beam passes through a solution containing an optically active compound, the rotation angle of the plane of polarization depends approximately linearly on the concentration of the compound. One can use this dependence for concentration measurements. The rotation angle (α) also depends on the wavelength (λ) of the incident light. The $\alpha(\lambda)$ function gives the ORD (optical rotation dispersion) spectrum. The right circularly polarized light is differently absorbed from the left circularly polarized light by optically active compounds. The different absorption is also wavelength dependent, and this dependence gives the CD (circular dichroism) spectrum. The ORD and CD spectra are characteristic properties of the optically active molecules, and their measurements provides an excellent tool for structure analysis of complicated organic molecules (Crabbé, 1972; Damjanovich, 1976; Garay, 1970).

***L* and *D* enantiomers**

The two enantiomers of optically active compounds are denoted by the *L* and *D* letters. They come from the Latin words laevus (left) and dexter (right), by convention, and have nothing to do with the direction of the plane rotation (both the *L* and the *D* enantiomers can have + and $-$ rotation properties).

The *D* and *L* enantiomers of the glyceraldehyde have the following configurations:

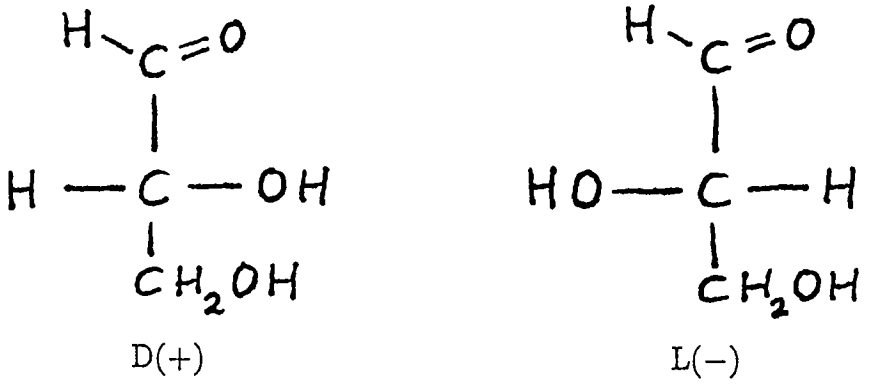


Figure 4

The absolute configuration (the spatial arrangement of the atoms) of the molecules can be determined by *X*-ray crystallography. This is, however, a rather difficult measurement. Fortunately, many molecular configurations can be traced back to the configuration of the glyceraldehyde.

The absolute configuration of the *L*-α-amino acids (the most important building blocks of life) is the following:

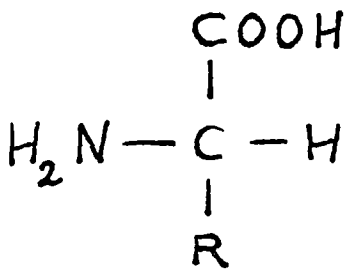


Figure 5

Here *R* denotes any groups of atoms. For the glycine, *R*=*H*, this molecule is optically inactive. The other α-amino acids have optical activity.

The *L* and *D* enantiomers of the optically active compounds have the same physical and chemical properties (except of the direction of optical rotation). This is the consequence of the mirror (space reflection) symmetry of the electromagnetic interaction (Glück, 1993; Section 3), since this interaction determines the chemical and the most important physical properties of the molecules. Laboratory synthesis of optically active compounds from inactive sources produces the *L* and *D* enantiomeric forms in equal quantity (the result of this synthesis is called racemic mixture of the compound or racemate).

2. BIOORGANIC OPTICAL PURITY (BIOMOLECULAR HANDEDNESS)

Living beings contain many optically active compounds (amino acids, sugars, etc.). *It is rather strange and puzzling, however, that they are built only from one enantiomeric form of these compounds. All living organisms use the same enantiomers*! For example, proteins are built only from *L*-α-amino acids, DNA (the carrier of the genetic information) contains only the D forms of sugars. We call this property of life *optical purity*. It could be one of the most important evidences of the common origin of life on the Earth.

Measurements of optical rotation and CD spectra show that proteins of living beings (with *L*-α-amino acids) have right-handed helical structure (α-helix).

Synthetic proteins built from *D*-α-amino acids have left-handed helix. Proteins built from amino acid racemate contain both *L*- and *D*-amino acids, and have either left- or right-handed helix. The growing rate of these mixed proteins is, however, 20 times slower than the growing rate of the pure proteins which contain either *L*- or *D*-amino acids only. Also, these mixed (*LD*) helices are unstable, and their catalytic activity is very feeble. On the other hand, the DNA and RNA molecules cannot be built from mixed nucleotides (containing both L and D sugars).

It seems from these and many other examples (Garay, 1970): *life requires almost perfect optical purity (chiral asymmetry).*

There are also many examples to show the connection between optical purity and biological organization. Cancerous tumours contain many *D*-amino acids. *D*-amino acids play an important role as components of bacterial cell walls. There are other inferior living beings (e.g.: funguses, insects) that contain also *D*-amino acids. It appears, however, that no *D*-amino acid has been isolated from a properly characterized protein, and that *D*-amino acids have not been isolated from mammals (Bentley, 1969; Garay, 1970).

Because of the chirality of its key molecules, human chemistry is highly sensitive to enantiomeric differences. An extreme example came to light in 1963 when horrible birth defects were induced by thalidomide. The defects were caused by the fact that whereas one enantiomer of this chiral compound cured morning sickness, the other caused birth defects. This example shows the importance of the separation of enantiomers in pharmaceutical industry. Another example is the limonene: one enantiomer of this compound smells like lemons, the other like oranges.

3. ORIGIN OF THE OPTICAL PURITY

Due to the mirror symmetry of the electromagnetic interaction, the chemical reactions are mirror symmetric. Therefore, the *L* and *D* enantiomers of chiral molecules arise from achiral molecules in equal amount. How could then the biomolecules have arisen with complete chiral asymmetry?

To answer this question, we distinguish two possibilities: the biomolecular asymmetry could have arisen either before or after the appearance of life.

(a) After the genesis of life

The first cell could have contained, by chance, proteins composed entirely of L-amino acids. This is, however, rather unprobable. Another possibility is that the first cell was created, also by accidental fluctuations, with a small excess of L-amino acids or D-sugars, and so incorporated only a slight chiral asymmetry. Then the total asymmetry developped by *natural selection*: the optical purity could be *selective factor* during the evolution (we have seen above: the biological processes favour the chiral asymmetry) (Hegstrom and Kondepudi, 1990).

(b) Before the genesis of life

(I) Spontaneous symmetry breaking, with perfect symmetry

Let us assume first that the physical and chemical processes have perfect chiral (mirror) symmetry. Paradoxical though it may seem, mirror-symmetric chemical reactions can produce, under special circumstances, unequal amounts of L and D enantiomeric forms through a phenomenon called spontaneous symmetry breaking. In this case, a symmetric state is one with equal number of L and D molecules; the asymmetric state is one in which one form dominates. Spontaneous symmetry breaking is a mechanism by which a system, with symmetric laws of nature, 'spontaneously' goes from a symmetric state to an asymmetric one (Lukács, 1993).

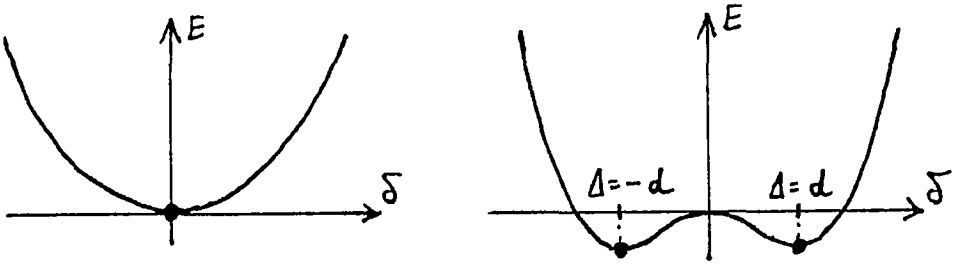
Let us consider the following model scheme of reactions (Hegstrom and Kondepudi, 1990; Kondepudi and Nelson, 1984); Kondepudi and Nelson, 1985):

$$A + B \quad \leftrightarrow \quad X_L \text{ or } X_D \qquad (1)$$
$$A + B + X_L \quad \leftrightarrow \quad 2X_L \qquad (2)$$
$$A + B + X_D \quad \leftrightarrow \quad 2X_D \qquad (3)$$
$$X_L + X_D \quad \rightarrow \quad P \qquad (4)$$

In this scheme, the chiral species X in the two enantiomeric forms X_L and X_D is produced from the achiral substrate A and B directly through reaction (1) and autocatalytically through reactions (2) and (3). X_L and X_D may also annihilate each other by producing a product P. With a suitable supply of the A and B compounds (to maintain their concentrations at a fixed level), the system can be driven far from the chiral symmetric state.

Let us define the δ asymmetry and the λ critical parameters of the system as:

$$\delta := (c_L - c_D)/(c_L + c_D); \qquad \lambda := c_A \cdot c_B$$



$a_2 > 0\ (\lambda < K) \quad : \quad \Delta = 0$ $\qquad$ $a_2 < 0\ (\lambda > K) \quad : \quad \Delta = \pm d$

Figure 6

Here c_L, c_D, c_A and c_B are the concentrations of the X_L, X_D, A and B compounds. Let us assume that the free energy of the system has the following δ dependence:

$$E(\delta) = a_2(\lambda)\delta^2 + a_4(\lambda)\delta^4$$

The system has perfect chiral symmetry: $E(\delta) = E(-\delta)$. The a_2 and a_4 coefficients may have the following λ dependences: $a_2(\lambda)=K-\lambda$, $a_4(\lambda) = \text{const}$. The system reaches its equilibrium when its free energy is minimal. As it is shown in the figures below, the $E(\delta)$ curve has only one minimum for $a_2>0$ ($\lambda < K$; $\delta_{min} := \Delta = 0$: symmetric state), and there are two minima for $a_2 < 0$ ($\lambda > K$; $\Delta = \pm d$).

For $\lambda < K$ the system is in chiral symmetric state. When λ is increased past the critical value K, the system will flop into a state where X_L or X_D is favoured, although which state is chosen is entirely random. The symmetry of the system for $\lambda > K$ is broken spontaneously (Lukács, 1993). For large λ the completely asymmetrical states ($\Delta = +1$ or $\Delta = -1$) will be reached:

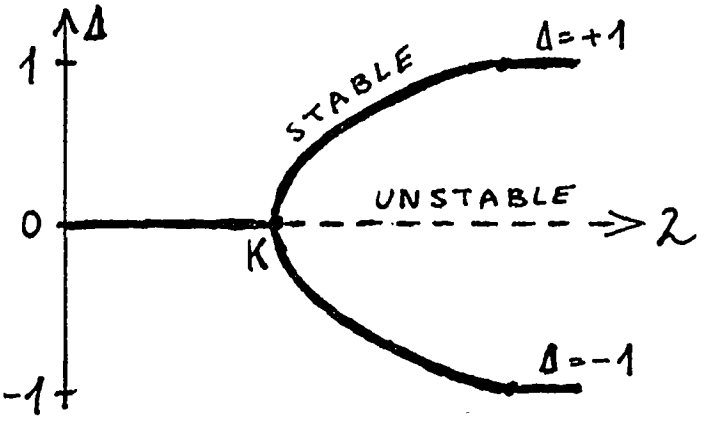


Figure 7

The $\Delta = 0$ state for $\lambda > K$ (dashed curve on Figure 7) is unstable.

Since the chiral symmetry of the system in this model is perfect, the final L or D dominance for large λ will be accidental: the system chooses either the $\Delta > 0$ or the $\Delta < 0$ direction at the $\lambda = K$ bifurcation point, but it is completely arbitrary which one of the two possibilities will be chosen: the L and the D dominance outcomes have equal (50 per cent) probabilities.

(II) Spontaneous symmetry breaking, with a small asymmetry

Let us add a small asymmetry term to the previous $E(\delta)$ function:

$$E(\delta) = a_2(\lambda)\delta^2 + a_4(\lambda)\delta^4 - \varepsilon\delta$$

The system is now asymmetrical: $E(\delta)$ is not equal to $E(-\delta)$. The figures below show the $E(\delta)$ curves for 3 different cases ($\varepsilon > 0$):

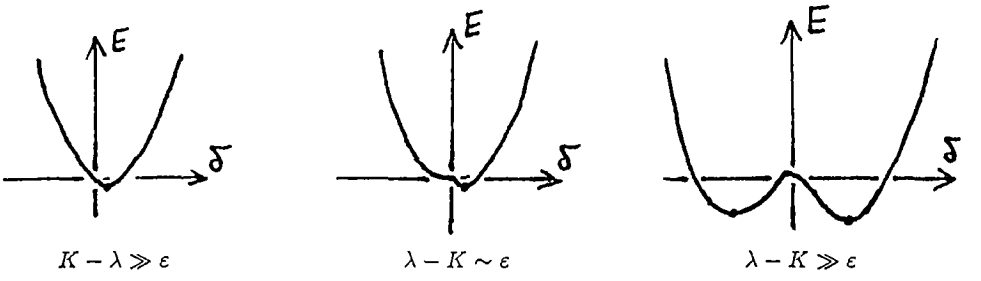


Figure 8

The system has some small preference for $\delta > 0$ (more L molecules than D molecules). The stable and unstable minima (Δ) have the following λ dependences now:

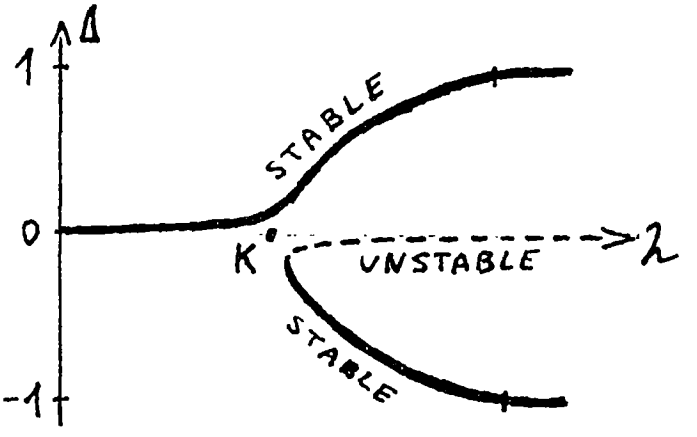


Figure 9

Let us increase the λ critical parameter. Then, if we neglect the statistical fluctuations, the system always goes into the $\Delta = +1$ asymmetrical state (with total L dominance). *The small chiral asymmetry of the system determines the direction of the chiral symmetry breaking* (Kondepudi and Nelson, 1985); Zeldovich and Mihajlov, 1987; Zeldovich, 1988).

If only mirror symmetrical (parity conserving) interactions were present in nature, then the particular choice of the dominance of the *L*-α-amino acids and the *D*-sugars in terrestrial organisms would appear to be a matter of chance. One could imagine another planet in the universe where the opposite enantiomers (*D*-amino acids and *L*-sugars) would dominate in living beings. There is an interaction, however, which has no mirror symmetry: the weak interaction. In the usual chemical processes its effect is much more weaker than the influence of the mirror symmetric electromagnetic interaction. The *weak interaction* can play, however, the role of the *small chiral asymmetry* in the spontaneous symmetry breaking of the biomolecules, thus *determining unambiguosly the dominant enantiomers.*

One possibility is the influence of the parity violating force mediated by the *Z* boson (Glück, 1993) (the so called weak neutral current) on the energy values of the quantum states of biomolecules. The effect of the *Z* force has been demonstrated experimentally for atoms, but not yet for molecules. An interesting theoretical result, however, has been obtained by S. F. Mason and G. E. Tranter. Between 1983 and 1986 they performed detailed calculations of the energies of several *L*- and *D*-amino acids, taking into account the asymmetric *Z* force. They found that, in all cases, the biologically dominant *L*-enantiomers have a lower ground-state energy than the corresponding *D*-enantiomers. The relative energy difference is of the order of 10^{-17} (Mason and Tranter, 1984; Mason, 1985). This effect seems to be very small when we take into account the statistical fluctuations. It has been shown by computer simulations, however, that under special conditions (*L* and *D* compounds competing with each other in 10^8 m^3 water, over a period of 10^5 years) the small systematic effect of the weak force overcomes the fluctuations, and determines the outcome of the symmetry breaking: nearly all the amino acid molecules will have the *L* enantiomeric forms (Hegstrom and Kondepudi, 1990; Kondepudi and Nelson, 1984); Kondepudi and Nelson, 1985).

Another possibility for the small chiral asymmetry could be the effect of the beta electrons coming from weak decays of radionuclides. These electrons are dominantly left-handed (their spin is opposite to their direction of motion), and the two enantiomers of a compound in a racemic mixture are differently decomposed by them (Ulbricht, 1959; Garay, 1970). The relative difference in the rates of such decomposition of *L*- and *D*-enantiomers could be about 10^{-6}. A. Garay had demonstrated experimentally this phenomenon (Garay, 1970; Garay, 1968).

Finally, we would like to make a remark on the connection between the handedness of the biomolecules and the chiral morphological asymmetries of the living organisms. These morphological asymmetries (like the difference between the left- and right-hand sides of the human brain) could have developped during the evolution by spontaneous symmetry breaking, if they gave some advantages to the organisms (i.e., these asymmetries appeared as selective factors for the biological evolution) (Holba and Lukács, 1993). *It might happen that in many cases the handedness of the biomolecules determined the directions of these morphological symmetry breakings* (similarly to the possible relationship between the parity violating weak interaction and the biomolecular handedness)

CONCLUSIONS

1. There are many organic molecules existing in two different forms related to each other as object and mirror image (optical isomers, enantiomers).

2. Optical purity (almost perfect chiral asymmetry of biomolecules) is a characteristic property of life: living organisms use only one form of the enantiomers (e.g.: *L*-amino acids, *D*-sugars).

3. Optical purity is necessary condition of life-functions.

4. Optical purity could have developped during the evolution of life by spontaneous symmetry breaking. The parity violating weak interaction might have unambigously determined the direction of this symmetry breaking.

5. The chiral morphological asymmetries of living organisms may be in causal relation with the chiral asymmetries of the biomolecules.

REFERENCES

Bentley, R. (1969) *Molecular Asymmetry in Biology*, New York: Academic Press.

Crabbé, P. (1972) *ORD and CD in Chemistry and Biochemistry*, New York: Academic Press.

Damjanovich, S. (1976) *Makromolekulák biofizikája*, [Biophysics of Giant Molecules, in Hungarian], Budapest: Akadémiai Kiadó.

Garay, A. (1968) Origin and role of optical isomery in life, *Nature*, 219, 318.

Garay, A. (1970) Optikai forgatóképesség biológiai jelentősége és eredete, [Biological significance and origin of ability for optical rotation, in Hungarian], *Fizikai Szemle*, 106.

Glück, F. (1993) Chirality in the elementary interactions, *Symmetry: Culture and Science*, 4, 1, 37-48.

Hegstrom, R. A. and Kondepudi, D. K. (1990) The handedness of the universe, *Scientific American*, 262, 1, 98.

Holba, Á. and Lukács, B. (1993) Hominid cerebral lateralisation as spontaneous symmetry breaking, *Symmetry: Culture and Science*, 4, 1.

Kondepudi, D. K. and Nelson, G. W. (1984) Chiral-symmetry-breaking states and their sensitivity in nonequilibrium chemical systems, *Physica*, 125A, 465.

Kondepudi, D. K. and Nelson G. W. (1985) Weak neutral currents and the origin of biomolecular chirality, *Nature*, 314, 438.

Lukács, B. (1993) On the mathematics of symmetry breakings, *Symmetry: Culture and Science*, 4, 1, 5-11.

Mason, S. F. and Tranter, G. E. (1984) The parity-violating energy difference between enantiomeric molecules, *Molecular Physics*, 53, 1091.

Mason, S. F. (1985) Biomolecular handedness, *Chemistry in Britain*, June, 538.

Ulbricht, T. L. V. (1959) Beta-decay and the biomolecular chirality, *Quarterly Review of Chemical Society*, 13, 48.

Zeldovich, Ya. B. (1988) Left-right asymmetry in biology, [Hungarian translation: Bal-jobb aszimmetria a biológiában, *Fizikai Szemle*, 222].

Zeldovich, Ya. B. and Mihajlov, A. C. (1987) Fluktuacionnaya kin'etika reakcij, [Fluctuational Reaction Kinetics, in Russian], *Uspekhi Fizicheskih Nauk*, 153, 469.